

REMARKS

Claims 1-23, 25 and 27 have been rejected in the Office Action. Claims 1, 6, 13, 15-18, 21-23, 25 and 27 are amended herein and claims 5, 12, 19 and 20 are canceled herein without prejudice or disclaimer to the subject matter herein to clarify the subject matter of the invention. Claims 1-4, 6-11, 13-18, 21-23, 25 and 27 are now pending in this matter.

The foregoing claim amendments are provided in the interest of furthering the prosecution of this application. No art has been cited against the claims and the claim amendments are not made for any reasons relating to patentability.

Basis for the claim amendments and newly added claims is found throughout the specification. Applicants believe that no new matter is submitted by these claim amendments. Accordingly, Applicants respectfully submit that the claim amendments should be entered.

CLAIM OBJECTIONS

In the Office Action, the Examiner objects to claims 19 and 20 as being of improper dependent form for failing to further limit the subject matter of a previous claim. Office Action, pages 2-3. The claims have been cancelled without prejudice or disclaimer to the subject matter therein, thus obviating the basis for the rejection. Applicants respectfully request that the Examiner reconsider and withdraw the objection.

REJECTION UNDER 25 U.S.C. § 101

In the Office Action, claim 22 is rejected as being directed to non-statutory subject matter. The Examiner asserts that claim 22, which recites a series of promoter sequences, appears to read on natural products. Office Action, page 3. The Examiner

indicates that "it would be remedial to amend the claim to read, 'an isolated promoter sequence selected from the group consisting of'. Office Action, page 4.

Claim 22 is currently amended to recite "an isolated promoter sequence" to clarify that the claims do not read on natural products, but instead recite promoter sequences that have been isolated from their native form, consistent with the Examiner's suggestion in the Office Action. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

REJECTION UNDER 35 U.S.C. § 112 SECOND PARAGRAPH

Claims 1-21, 23, 25 and 27 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants submit that the claims prior to their amendment herein were definite because persons skilled in the art would have been readily able to ascertain the scope of the claimed invention. Nonetheless, Applicants amended their claims in an effort to expedite prosecution of the application. The amendments are intended to merely add consistency to certain portions of the claims, and they are not related to patentability of the claims. The amended claims continue to satisfy the definiteness requirements of 35 U.S.C. § 112, second paragraph.

With regard to claim 1, the Examiner asserts that "the metes and bounds of the phrase 'said promoter sequences covering a range of promoter activities for said gene in small steps each step changing the activity by 50-100% . . .' are unclear." Office Action, page 12. The Examiner indicates that it would be "remedial to amend the claim language to clearly indicate whether the cell in which the promoter activity is determined necessarily is the same as the recited organism(s)." Office Action, page 12.

Applicants have amended claim 1 to clearly indicate that the cell in which the promoter activity is determined is the same as the recited organism(s) consistent with the Examiner's suggestion. In particular, Applicant's have amended the claim to recite

"said set of promoter sequences covering a range of promoter activities for said gene in said selected microorganism". Accordingly, Applicants respectfully submit that this amendment obviates the foregoing basis for the rejection of claim 1 and the claims that depend therefrom.

The Examiner also asserts that claim 1 is "vague and indefinite in that it is unclear whether the sentence ' . . . between said consensus sequences of flanking . . . consisting of the nucleobases A, T, C and G . . .' refers to both eukaryotic and prokaryotic promoter sets." Office Action, page 12. The Examiner indicates that "it would be helpful to amend the claim structure such that the eukaryotic and prokaryotic elements are clearly separated and so that those limitations which refers to both types of promoter sets clearly related to both types." Office Action, pages 12-13. Applicants have amended claim 1 consistent with the Examiner's suggestion, thus obviating the basis for rejection.

With regard to claim 16, the Examiner asserts that "the metes and bounds of the words 'or both' in part (i)-line 5 are unclear." Office Action, page 13. Also with regard to claim 16, the Examiner indicates that there is no antecedent basis for the words "the set of promoter sequences covering a range of promoter activities for said gene." Office Action, page 13. Applicants respectfully submit that the foregoing amendments to claim 16 overcome the Examiner's basis for rejection.

With regard to claim 17, the Examiner asserts that the claim "merely recites a desired outcome . . . without any action steps that would necessarily give the desired result." Office Action, page 13. Applicants have amended claim 17 to recite an action step. In particular, the claim has been amended to recite "a plurality of promoter sequences is selected from the set of promoter sequences, said plurality of promoter sequences covering a range of promoter activities for said gene, in steps, each step changing the promoter activity by 50-100%." Accordingly, Applicants respectfully submit that the amendment obviates the Examiner's basis for the rejection.

With regard to claims 18 and 21, the Examiner indicates that there is a lack of proper antecedent basis. Applicant's respectfully submit that the amendments to claims 18 and 21 clarify that proper antecedent basis is provided and thus obviate the Examiner's grounds for rejection.

In view of the foregoing amendments and remarks, Applicants respectfully request that the Examiner reconsider and withdraw the rejection. The Examiner is welcomed to contact the undersigned, if further clarification in the claims is believed to be required.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH
(LACK OF ADEQUATE WRITTEN DESCRIPTION)

Claims 1-15, 18-20, 23, 25 and 27 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

At the outset, applicants respectfully point out that the initial burden of establishing a basis for denying patentability of a claimed invention rests upon the Patent Office. *See In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). It is equally well established that the Patent Office bears the initial burden to establish a reasonable basis to question the written description provided in the specification for the invention defined in Applicants' claims. *See In re Wright*, 27 U.S.P.Q.2d 1510 (Fed. Cir. 1993).

Applicants respectfully traverse the Examiner's rejection for the following reasons. Applicants' full scope of claimed subject matter was described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, prior to the amendment of the claims herein. Nonetheless, in the interest of advancing prosecution, applicants amended their claims. Applicants' claimed subject matter continues to be

described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

It is well established that a disclosure of the specification provides a description of the claimed subject matter if it reasonably conveys to persons skilled in the art that the inventor has possession of that subject matter at the time the application was filed. *See, e.g., Fujikawa v. Wattanasin*, 39 U.S.P.Q.2d 1895 (Fed. Cir. 1996) and *Vas-Cath, Inc.v. Mahurkar*, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). Applicants respectfully submit that their specification, as filed, satisfied that standard because persons of ordinary skill in the art, familiar with applicants' specification, would clearly understand that they possessed the claimed subject matter. This is indicated, for example, by the Examiner's appreciation of the full scope of Applicants' claimed invention in the Office Action.

In the Office Action, the Examiner asserts that the claims comprise a set of promoters that can be derived from any source to drive expression of any gene in any organism or any combination of organisms. See Office Action, page 5. However, the foregoing claim amendments clarify that the claimed set of promoter sequences is directed to *microorganisms*. Further, as previously noted, the promoters are structurally and functionally characterized. The structural limitations of the claims include the requirement that each promoter sequence of the set of promoters comprises a double stranded DNA sequence, the sense strands of which comprise at least two conserved sequences *identified in said microorganism* and the conserved sequences are restricted to specific sequences for prokaryotic and eukaryotic organisms, respectively, and the functional characterization requires that any given set of promoters cover a range of promoter activities in steps, each step changing the promoter activity by 50-100%.

Under the current Written Description Guidelines of the U.S. Patent and Trademark Office (Patent Office), one way in which the written description requirement for a claimed genus may be satisfied is by disclosure of "relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by

functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." 66 Fed. Reg. 1099, 1106 (2001). Here, the claims specifically recite structural characteristics (i.e., a double stranded DNA sequence, the sense strands of which comprise at least two conserved sequences *identified in said microorganism* and the conserved sequences are restricted to specific sequences for prokaryotic and eukaryotic organisms, respectively) and functional characteristics (i.e., a range of promoter activities in steps, each step changing the promoter activity by 50-100%) and that this is coupled with a "disclosed correlation between function and structure" (i.e, a set of sequences that optimizes expression of a gene in a selected microorganism). Therefore, based upon the Patent Office's own Guidelines, the specification satisfies the written description requirement.

Further, as has been previously noted, the new Written Description Guidelines specify that one of the factors to be considered in determining if the written description requirement is satisfied is whether a representative number of species is disclosed in the specification. (See Guidelines, page 9). A representative number of species is disclosed if one skilled in the art would recognize that applicant possessed the necessary common attributes or features of the elements of the members of the genus in view of the species disclosed and claimed. *Id.*

As clearly demonstrated by a review of the specification, and contrary to the Examiner's assertion, Applicants do indeed disclose such a representative number of species. Several examples show the promoter sets for various *microorganisms*. For instance, Examples 1 and 2 on pages 17 to 27 of the specification specifically provide a set of promoter sequences for *L. lactis*, and Example 7 on pages 31-34 of the specification specifically provide a set of promoter sequences for *Saccharomyces cerevisiae*. Further examples are provided concerning other bacteria, such as *Bacillus subtilis*, *Pseudomonas* and *E. coli*, and various exemplary methodologies for constructing the promoter sequences in accordance with the claimed invention, as well.

As has been previously noted, the broad applicability of Applicants' invention represents the type of innovation the patent system seeks to encourage. To deny Applicants a patent on the basis that their invention may be applied to a large number of desired microorganisms is tantamount to denying them a patent because their invention is too effective and useful. Such a result is clearly contrary to United States patent law. It is well established that inventors may claim their inventions generically. Therefore, a person of skill in the art would reasonably conclude Applicants were indeed in possession of the claimed invention.

Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH
(LACK OF ENABLEMENT)

It is well established that the test for enablement is whether one of ordinary skill in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988); see also *United States v. Teletronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988).

In the Office Action, the Examiner rejects claims 18 and 20 under 35 U.S.C. § 112, first paragraph. The Examiner alleges that "the specification, while being enabling for embodiments featuring promoter sets that regulate expression of a desired gene in an organism, does not reasonably provide enablement for any embodiment wherein the flux of a cellular metabolite is controlled." Office Action, page 9. Applicants respectfully submit that the foregoing amendments obviate the rejection and respectfully traverse for the reasons stated below.

As it will be appreciated, the starting point for a person skilled in the art in setting out to construct a promoter set as claimed in a given microorganism is to

identify at least two conserved sequences (as defined in the claims) in said microorganism. To identify such conserved sequences is well within the common knowledge of the skilled artisan and evidently, the measures to carry out such an identification using conventional methods are not dependent on the particular type or species of organism. After having provided a set of promoters wherein each promoter sequence comprises the conserved sequences as identified by randomly incorporating nucleotides in spacer sequences, the ordinarily skilled artisan may select a number of promoters to provide a set of promoters having the functional characteristic of covering a range of promoter activities in steps, each step changing the promoter activity by 50-100%. Again, the selection of such a set of promoters does not require any inventive skills, but can be performed using conventional methods which are well known in the art.

As would also be appreciated, there are no difficulties in providing the claimed set of promoters for any given microorganism. The invention does not primarily lie in the construction of the set of promoters, but rather in that the inventor realized that (1) by randomly changing the sequence of spacer sequences, the promoter strength could be varied to provide promoters having a wide range of promoter activities and (2) the realization that the expression of a given gene in the selected microorganism could be optimized by replacing the natural promoter with one of the constructed promoter set and that the promoter resulting in an optimized expression of the gene is not, as generally believed in the art, necessarily that having the strongest promoter activity. The crux of the invention is, therefore, that it has become possible to optimize gene expression in any given microorganism using a set of promoters covering the range of activities as defined in the claims. Accordingly, a person skilled in the art, guided by such disclosures would be able to make and/or use the claimed class of promoter sets, without undue experimentation. In *In re Wands*, the Federal Circuit held that the specification was enabling with respect to the claims at issue because "there was

considerable direction and guidance in the specification". *Id.* Here, as in Wands, there is considerable direction and guidance in the specification.

Therefore, it is submitted that a person of ordinary skill in the art can practice the full scope of the claimed subject matter without having to conduct any undue experimentation. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

REQUEST FOR ALLOWANCE

For at least the reasons detailed above, Applicants respectively submit that all of the claims in the application are patentable. Favorable consideration, entry of this amendment, and issuance of a notice of allowance are respectively requested.

In the event any issues remain, the Examiner is encouraged to contact applicants' representatives to resolve such issues in an expeditious manner, and place the application in condition for allowance.

In the event any fees are incurred upon the filing of these documents, please charge the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

HUNTON & WILLIAMS

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